REMARKS

Claims

Claims 1-13 are pending. Claims 1-3, 6 and 9 are amended. Support for claim 1 as amended can be found, for example, at page 7, para. 6. Additionally, amendments to claims 1-3, 6 and 9 were made for the purposes of clarification.

35 USC §102(b) rejection

Claims 1-13 are rejected as allegedly being anticipated by Lexow (WO0161036A2). Applicant respectfully disagrees. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See MPEP §2131 citing Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The claims have been amended so that they are directed to a method of manufacturing nucleic acids by including in the body of the claim, e.g., in steps (a) and (b) that the first and second oligonucleotides are a part of a nucleic acid to be manufactured and in step (f) that the steps (a) to (e) are repeated at least, whereby the elongated first oligonucleotide of step (d) is further elongated.

Lexow et al. does not anticipate the present claims as it fails to teach a method of further elongating an oligonucleotide, by ligating an additional second at least partially double-stranded oligonucleotide and cutting the further ligation product with a type IIS restriction enzyme and releasing a further elongated oligonucleotide. Lexow et al. at pages 11-12, Figure 6 and claim 7 teaches ligating the nucleic acid fragment/overhang-adaptor complex, where the nucleic acid fragments were ligated at their *first ends* to the overhang-adaptor (see claim 7 (d1), and page 11, line 27 of Lexow), with a second set of overhang-adaptors, where the second set of overhang adaptors are ligated at the *second ends* of the nucleic acid fragments (see claim 7 (d2), and page 12, line 15 of Lexow) and identifying the sequence of the first and second overhanging ends of the nucleic acid fragments. This fails to anticipate the present claims as in Lexow et al, the first and second set of overhang-adaptors are ligated to opposing ends (the first ends and the second ends) of the nucleic acid fragment, which is most clearly depicted in Figure 6 of Lexow. In Lexow et al, the purpose for the two sets of overhang-adaptors being ligated to opposing ends of the nucleic acid fragment is so the overhang-adaptors can be used to identify the sequences of the nucleotides of both overhangs.

The present claims, however, describe a method of manufacturing nucleic acids, where the building blocks of oligonucleotides are added only to one side of the elongated nucleic

acids, not to opposing ends as in Lexow et al. This is most clearly depicted in Figure 1 of the present specification. This is specified in claim 1 as follows: step (c) states that the first and second oligonucleotides are ligated via the first single stranded overhang of the first oligonucleotide and the single-stranded overhang of the second oligonucleotide. The second single-stranded nucleotide overhang of the first oligonucleotide (first modification) is not ligated to another oligonucleotide, but as step (c) describes, the second single-stranded nucleotide overhang of the first oligonucleotide (first modification) allows the immobilization of the first ligation product to a surface.

Based upon the present amendments to the claims, Applicant respectfully requests Examiner to withdraw this rejection.

In the Advisory Action mailed July 14, 2011, Examiner alleges that claims 1-13 are anticipated under §102(b) by Lexow et al. for the following reasons. Applicant will respond to each one in turn.

First, Examiner argues that the target nucleic acid fragments ligated to the adapter overhangs and the ligated product reads on an elongated fragment. Applicant respectfully disagrees. The present claims do not include the ligated product prior to being cut with a restriction endonuclease within the scope of the term elongated fragment. Claim 1 step (c) states that there is a ligation forming the first ligation product. Claim 1 step (d) specifies that the first ligation product of step (c) is cut with the first type IIS restriction enzyme, releasing an elongated oligonucleotide. In Lexow et al., the majority of examples teach the cutting of the nucleic acid fragment/overhang-adaptor complex and the result is the same nucleic acid fragment as before, therefore, the nucleic acid fragment is not elongated. See Figure 2 of Lexow. This makes sense as Lexow describes a method of sequencing, specifically sequencing the overhangs created by type II restriction endonucleases. See page 1, lines 17-20 of Lexow. In Figure 6 of Lexow et al., however, the nucleic acid fragment/overhang-adaptor complex was cut and the resultant fragment was larger, but there the nucleic acids were not cut by a type IIS restriction enzyme, as DraI is not a type IIS enzyme. In addition, as discussed above, Lexow et al. does not disclose repeating the steps (a) to (e) at least once whereby the elongated first oligonucleotide of step (d) is further elongated, as is presently claimed.

Second, Examiner argues that the overhang-adaptor ligated target nucleic acid when released from the solid support with a type IIS restriction enzyme produces one longer fragment and one shorter fragment. Examiner cites 11, lines 21-36 here. This passage is distinguished above, and does not anticipate the present claims for the reasons provided

therein. Regarding Examiner's citation of page 8, lines 37-38 and page 9, lines 1-10, applicant does not appreciate how these passages are related to releasing a nucleic acid from a solid support and producing unequal fragment sizes. Additionally, Figure 2 shows that the overhang-adaptor ligated target nucleic acid is released from the solid support using SapI, a type II restriction enzyme. There the Target DNA is not elongated. The Target DNA only starts with a 4 nucleotide overhang in step 1), is ligated to the overhang-adaptor, and then is cut with SapI, a type IIS restriction enzyme, in order to create a 3 nucleotide overhang (step 4) and 5)), so that the overhang can be readily sequenced.

Fourth, Examiner argues that Lexow et al. teaches a modification as the ligated fragments comprise a binding moiety to enable attachment to a solid support. The teachings of Lexow et al., however, do not anticipate the present claims as Lexow et al. does not teach that the modification can be a single-stranded nucleotide overhang, as claimed.

For the above reasons, applicant respectfully requests that the §102(b) rejection over Lexow et al. is withdrawn.

35 USC §102(e) rejection

Examiner alleges that claims 1-13 are anticipated under §102(e) by US20060194202 because claim 1 step (c), which states "wherein the modification of the first ligation product essentially corresponds to the second single-stranded overhang" does not necessarily read on a modification as a single-stranded overhang, rather it could be a streptavidin that corresponds to a biotin, especially, as claims 9-11 read on biotin. The claims have been amended and applicant believes clarified so that the term *first modification* in claim 1 does not include biotin. Therefore, applicant believes this rejection to be overcome and respectfully requests that it be withdrawn.

Final office action mailed April 28, 2011

Applicant believes that this reply is responsive to all of Examiner's rejections outlined in the Advisory Action mailed on July 14, 2011. In addition, the reply to the Final Office Action (mailed on April 28, 2011) that was filed by Applicant on June 28, 2011 was entered by Examiner, therefore, Applicant believes that this reply satisfies the submission requirement of 37 CFR §1.114.

Request for an Interview

Applicant respectfully requests an interview with Examiner at the earliest possible convenience. As attorney for applicant is located outside of the United States, the Examiner cannot reach applicant's representative by phone. If Examiner is willing to provide an Interview prior to the mailing of the first office action on the merits, please contact the applicant's representative at the email address provided below.

CONCLUSION

In view of the foregoing arguments/amendments, Applicant submits that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-4520. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. §1.136(a)(3).**

Respectfully submitted,

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